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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/883,842	06/18/2001	Stanley Stein	601-1-097 N	9975

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DAVIDSON, DAVIDSON & KAPPEL, LLC
485 SEVENTH AVENUE, 14TH FLOOR
NEW YORK, NY 10018

EXAMINER	
FUBARA, BLESSING M	
ART UNIT	**PAPER NUMBER**
1618	

DATE MAILED: 11/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/883,842	STEIN ET AL.	
	Examiner	Art Unit	
	Blessing M. Fubara	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-28,31-34 and 38-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5-28, 31-34 and 38-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of amendment, remarks and request for extension of time, all filed 08/29/05. Claims 1, 5-28, 31-34 and 38-57 and new claims 58-61 are pending.

Claim Rejections - 35 USC § 102

1. Claims 1, 5, 6, 13-19, 21, 25-28, 33, 38-40, 43-53, 55 and 56 remain rejected under 35 U.S.C. 102(b) as being anticipated by Roos et al. (US 5,840,338) and new claims 58 –60 are included in the rejection.

Applicants argue that Roos does not disclose that the matrix forms a hydrogel matrix after injection into a mammal such that the at least one therapeutic agent is released in a controlled manner from said hydrogel and that the method of claim 19 forms a cross-linked matrix after injection.

2. Applicants' arguments filed 08/29/05 have been fully considered but they are not persuasive.

The composition of the prior art like the instant composition contains polymer networks comprising biologically active agents and cross-linking agents, and the composition is formulated as an emulsion or injectable suspension. The composition injected by the claims read on the composition of Roos. According to MPEP 2112.01 [R-2], II, "products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990)." Therefore, both the composition of the prior art and the claims would undergo the same fate when injected. New claims 58-60 limit the

compositions to include cross-linking agents and the composition of Roos contains cross-linking agents. Cross-linking in the method of claim 19 takes place after injection and since Roos administers the composition containing cross-linking agent and responsive polymer by injection, the composition undergoes cross-linking to form a gel at the site. (See rejection below).

Roos discloses polymer gel networks that are loaded with biologically active solutes (abstract). The biological agents that can be loaded in the polymer networks of Roos are listed in column 52, line 15 to column 56 line 18 and some of the specific examples are anti-depressants, muscle relaxants, opioids, anti-cancer agents, antibiotics, anti-viral agents, antihistamines, anti-aids substances and neurotransmitters. The polymers are selected from polyvinyl alcohol, dextran, polyvinylpmolidone, polyethylene oxide and polypropylene glycol and polyethylene glycol (column 13, lines 33-38) and the gel is a 3-D cross-linked polymer network (column 13, lines 46-48; column 14, lines 13-27). The polymer network of Roos can be an emulsion, draught, syrup, elixir or powder or granules or liposomes or capsules or cachets or tablets or lozenges (column 36, lines 10-15). Roos meets the limitations of the claims.

3. Claims 1, 5-7, 8, 11-21, 23, 25-28, 33, 34, 38-40, 43-47, 49-53, 55 and 56 remain rejected under 35 U.S.C. 102(b) as being anticipated by Grinstaff et al. (US 5,498,421); and new claims 58-60 are included in the rejection.

Applicants argue that Grinstaff do not disclose a matrix that is an emulsion where the therapeutic agent is contained in the oil phase because the therapeutic agent in Grinstaff is contained in the polymeric shell and "would not be physically entrapped within a hydrogel matrix;" that Grinstaff cannot anticipate claim 19 because cross-linking takes place after

injection in the claims and Grinstaff does not disclose an emulsion containing a matrix according to claim 19 (ii).

4. Applicants' arguments filed 08/29/05 have been fully considered but they are not persuasive.

Figure 1 of Grinstaff is a polymeric shell and the emulsion within the shell contain biologic (column 7, lines 31-42) and specifically, the emulsion is referred to as water-in-oil emulsion. The shell is cross-linked via disulfide bridges and the presence of sulfhydryl meets the limitation of cross-linking agent since it the oxidation of the sulfhydryl groups that lead to the cross-linked shell. The shell is depicted in Figure 1 and contains a matrix. Grinstaff discloses that the suspension containing the polymeric shell, which in turn contains the emulsion that contains the biologic is administered intravenously (column 6, lines 58-67; column 7, line 17). In Grinstaff, a double emulsion technique can be employed to encapsulate the biologic in the polymeric shell. Since the composition of the prior art and the claimed invention are the same, then composition of the prior art would also undergo cross-linking after injection.

The claims are broad and do not recite any specific cross-linking agent and amounts. (See rejection below).

Grinstaff provides compositions for in vivo delivery of solid or liquid active agents contained in cross-linked polymeric shells, through several routes of administration, including oral, subcutaneous, intraperitoneal and transdermal (col. 7, line 60 to col. 8, line 33). Grinstaff includes linear and branched PEGS among the synthetic polymers used in the invention, and teaches that the active agent may be dispersed in oil and the polymeric shells containing the

active agent may be suspended in an aqueous medium to form lipid-containing emulsions (column 9, line 14 to column 10, line 2). Grinstaff discloses that the polymeric shell can be modified by forming a covalent bond with cross-linked polymers such as PEG derivatives, including PEG-thiols (col. 12, line 14 to col. 13, line 27). Grinstaff et al. teaches that the compositions of the invention are suitable for delayed or controlled release of an entrapped pharmaceutical agent (Example 5). Grinstaff discloses in column 9, lines 14-22, that "polyalkylene glycols (e.g., linear or branched chain), polyvinyl alcohol, polyhydroxyethyl methacrylate, polyacrylic acid, polyethyloxazoline, polyacrylamide, polyvinyl pyrrolidinone, and the like, are good candidates for chemical modification (to introduce sulfhydryl and/or disulfide linkages) and shell formation (by causing the cross linking thereof." Biologic agents delivered by the system of Grinstaff are analgesic agents, anesthetic agents, anti-asthmatic agents, antibiotics, anti-depressant agents, anti-diabetic agents, anti-fungal agents, anti-hypertensive agents, anti-inflammatory agents, anti-neoplastic agents, anxiolytic agents, enzymatically active agents, nucleic acid constructs, immunostimulating agents, immunosuppressive agents, physiologically active gases, vaccines, and the like, diagnostic agents (such as ultrasound contrast agents, radio-contrast agents, or magnetic contrast agents), and agents of nutritional value, and the like (column 8, lines 24-33). Grinstaff meets the limitations of the claims.

5. Claims 1, 38, 40 and 43-51 remain rejected under 35 U.S.C. 102(b) as being anticipated by Yanaki et al. (US 5,538,728); and new claims 58 and 60 are included in the rejection.

Applicants argue that Yanaki does not disclose a composition as recited in claims 1 and 38; the instant compositions form hydrogel upon injection and the composition of Yanaki does not do that.

6. Applicants' arguments filed 08/29/05 have been fully considered but they are not persuasive.

Yanaki's composition contains cross-linking agent (column 3, lines 42-63). The composition of Yanaki is an emulsion (Example 25). The claims are directed to broad subject matter that reads on the prior art composition. According to MPEP 2112.01 [R-2], II, "products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990)." Therefore, both the composition of the prior art and the claims would undergo the same fate when injected.

(See rejection below).

Yanaki discloses hydrogel composition (column 7, lines 21-25, 62-65; column 8, lines 3-11) that contains polysaccharide (column 3, lines 24-26), cross-linked polymer, cross-linked dextran (column 3, lines 52-65), polyethylene glycol (column 11, line 2., column 13, line 39), pharmaceuticals such as antibiotics (column 12, lines 20-42); the composition can be an emulsion (column 28, line 22); the composition can be administered rectally (column 9, line 40; column 10, line 16). The release order recited in claim 45 is an inherent property of the composition. Yanaki meets the limitations of the claims.

Claim Rejections - 35 USC § 103

7. Claims 31 and 32 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Roos et al. (US 5,840,338).

Applicants argue that Roos does not disclose the method of claim 19 and thus cannot render obvious claims 31 and 32 that depend from claim 19.

8. Applicants' arguments filed 08/29/05 have been fully considered but they are not persuasive.

Cross-linking in the method of claim 19 takes place after injection and since Roos administers the composition containing cross-linking agent and responsive polymer by injection, the composition undergoes cross-linking to form a gel at the site. Thus claims 31 and 32 depending from claim 19 are rendered obvious by Roos.

Claim Rejections - 35 USC § 112

9. Claims 1, 5-28, 31-34, 38-57 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. New claims 58-61 are included in this rejection.

Applicants argue that polyamino acids are well known in the art to the skilled artisan and as such no disclosure of polyamino acids is required.

10. Applicants' arguments filed 08/29/05 have been fully considered but they are not persuasive.

While polyaminoacids are known to the skilled artisan, without a disclosure and appropriate guidance, it would inflict tremendous burden on the skilled artisan to through extensive experimentation determine those polyaminoacids that may be applicable in the invention. Lysine is not a polyaminoacid.

Examiner acknowledges applicants' explanation regarding the question on the α,ω-dihydroxy-PEG and α,ω-diamino-PEG or the product formed from α,ω-dihydroxy-PEG and thiomalic acid or α,ω-diamino-PEG and thiomalic acid and α,ω-dicarboxy-PEG and lysine.

Examiner further acknowledges applicants' explanation on the Request to add an inventor, in the explanation, applicants indicated that the appropriate/necessary forms would be provided in the future for the change of inventorship of the invention.

No claim is allowed.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 3:30 p.m. (Monday to Friday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BF

Blessing Fubara
Patent Examiner
Tech. Center 1600

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600